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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,750	11/15/2001	Ronald Vogels	2183-5148US	5853

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EXAMINER
BURKHART, MICHAEL D

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,750	VOGELS ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/16/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,33-40,43 and 44* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 38-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-22,33-37,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11/15/2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Sequence Compliance

Figures 5 and 38 contain sequence disclosures not identified by a SEQ ID number in the figures or in the Brief Description of the Drawings. A SEQ ID number should be specified for the nucleotide limitation in claim 22. The references to SEQ ID's in the specification on pages 22-28, 30, 32, 33, 38, 43, 46, 47, 52-54, and 58 do not contain SEQ ID numbers. These details are requirements of the Sequence Rules (MPEP 2400 §1.821-1.825) and must be corrected. Any response which does not include compliance with the Sequence Rules will be considered non-responsive.

Priority

Acknowledgment is made of applicants claim for priority based on application 09/713,678, filed on 11/15/2000, now U.S. patent 6,492,169, issued 12/10/2002.

Election/Restrictions

Applicants election of Group II (claims 34-37) without traverse, filed 4/13/2004, is acknowledged. Claims 4-22, 33, 43 and 44 were amended to depend from the elected group.

Claims 1-3 and 38-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 23-32 and 41-42 were previously canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention appears to employ the PER.C6 cell line, deposited as ECACC No. 96022940. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, a deposit of the biological materials may satisfy the requirements of 35 U.S.C. § 112. The specification does not disclose a repeatable process to obtain the biological material and it is not apparent if the biological materials are readily available to the public. It is noted that Applicant has deposited the biological materials, but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon an issuance of patent, would satisfy the deposit requirement made herein. If the deposit has

not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. §§ 1.807); and

(e) the deposit will be replaced if it should ever become unviable.

Applicant's attention is directed to M.P.E.P. § 2400 in general, and specifically to §2411.05, as well as 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information.

Claims 15, 16, 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for human adenovirus vectors that transform primary human

cells and may be complemented by the transformed cells, does not reasonably provide enablement for vectors derived from bovine adenovirus (BAV hereafter) that are expressed and/or complemented in human cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. The art concerning transformation of human cells with BAV E1B-55k and the production of recombinant BAVs in human cells is unpredictable. Because full transformation by adenoviral E1 proteins requires both E1A and E1B sequences, it is not predictable that human cells could be transformed if BAV E1B-55k replaces human adenovirus E1B-55K. Adenoviruses have evolved to orchestrate a delicate interplay with host proteins in order to replicate efficiently. This interplay is disrupted when the host is changed, therefore it is unpredictable that a recombinant BAV could be complemented in human cells. See, for example, van Olphen et al. (J. of Virology; 76 p.5882-5892: 2002 and Virology; 295 p.108-118: 2002) and references therein establishing that human 293 cells cannot complement E1-deleted BAV.

State of the art. The state of the art regarding the production of recombinant bovine adenoviruses from human cells, even those expressing BAV E1 proteins, is poorly developed. The development of such human cells would have to be done empirically, along with the development of the appropriate BAV vectors.

Number of working examples. Applicants have provided no working examples of human cells expressing BAV E1B-55K that complement recombinant BAVs.

Amount of guidance. Applicants provide no direction or vector diagrams for the claimed BAV E1B-55K or complementing recombinant BAV. The specification requires the skilled artisan to practice trial and error experimentation with different BAV subgroups, vectors and human cell lines to determine which (if any) will be compatible as claimed.

Scope of the invention. The claims are broad in nature and read on any BAV sequence from any subgroup.

Nature of the invention. The invention involves the unpredictable art of producing recombinant BAV from human cell lines.

Level of skill in the art. While the level of skill in the art is high, the unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Claims 15, 16, 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim methods to transform primary, diploid human cells with human adenoviral E1 proteins and/or BAV E1B-55K, then produce complemented recombinant human adenoviruses or BAVs using the cells. Applicants disclose methods to transform human cells by expressing human adenoviral E1A and E1B proteins that are derived from a different subgroups (E1A from subgroup C and E1B from subgroup B, for example). This is done to allow efficient transformation of human cells and to allow a broader complementation of recombinant adenovirus by these same cells. The claims read on a genus of methods to produce recombinant non-subgroup C human adenoviruses and BAVs from human cells transformed as described above.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. In the instant case, applicants only disclose the human adenoviral E1A/E1B vectors and cells necessary for transformation and complementation

of recombinant human adenoviruses. Neither applicants nor the prior art disclose BAV E1B proteins capable of transforming human cells or human cells capable of complementing recombinant BAVs. Applicants claim the process of using BAV E1B-55K and human cells to complement recombinant BAV by function only, without a correlation between structure and function. Applicants provide no disclosure of which subgroup of BAV is involved, nor what precisely a recombinant BAV would consist of (for example, is E1 deleted?). Given the diversity of human adenoviruses and BAVs and the failure of the human 293 cell line to complement E1-deleted BAV (van Olphen et al., J. of Virology; 76 p.5882-5892), it is unpredictable that BAV E1B-55K could contribute to the transformation of human cells or that recombinant BAVs be complemented by the same. The diversity of the adenoviruses involved, lack of disclosure regarding which BAV subgroups and sequences should be used and which human cells should be used, would require the skilled artisan to conclude that the examples presented by the applicants are not sufficient to describe the claimed genus.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-22, 33-37, and 43-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 is vague and indefinite for reciting, " derived" and "derivatives thereof". It is not clear what the "derivative" of a primary human cell would be in this case. It is unclear how

closely related to the original starting cells the "derivatives" are. The metes and bounds of the claimed subject matter are unclear. This rejection affects all dependant claims.

Regarding claim 11, the phrase "more particular" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 16 and 44 recite the limitation "complementing recombinant adenovirus" in line 2 of each claim. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 5-14, 17, 34, 36, and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,492,169 ('169 hereafter). Although the conflicting claims are not identical, they are not patentably distinct from each other because the process for complementing a recombinant adenovirus in the instant claims is rendered obvious by the packaging cell line claimed in '169. The instant claims recite a process to complement a recombinant adenovirus, based on subgroup

B or type 35, by providing a primary, diploid human packaging cell line that has been transformed by adenovirus E1 coding sequences, either operatively linked on one molecule or located on two separate molecules. The E1 coding sequences can be selected from different subgroups of adenovirus, to provide a chimeric E1 construct with the properties of efficient transformation and serotype-specific complementation. In this chimeric construct, the E1A and part of the E1B-22K sequence can be from subgroup C adenovirus while the E1B-55K sequence is from subgroup B or type 35. Also in this chimeric construct, the E1 sequences can be from subgroup C adenovirus, except those E1B-55K sequences necessary for serotype-specific complementation. The '169 patent recites packaging cells with identical characteristics (claims 1-7), that are "capable of complementing recombinant adenoviruses" (claims 1-3). Because the packaging cells of the '169 patent are designed to be used for complementing recombinant adenoviruses (as stated above), the instant process claims are rendered obvious over the '169 composition claims.

The closest prior art is exemplified by Abrahamsen et al. (J. Virol., 1997; 71 (11): 8946-8951) and Falck-Pedersen (5,849,561). Abrahamsen et al. teaches the complementation of an E1A-deleted adenovirus type 7a (Subgroup B) by HEK-293 human embryonic kidney cells. The HEK-293 cells express adenovirus E1 proteins. Abrahamsen et al. do not teach the use of adenovirus type 35.

Falck-Pedersen teaches a method to produce and harvest non-subgroup C adenoviruses by use of a packaging cell that expresses the E1 and E4 gene products of a different serotype than the adenovirus vector. The adenovirus vector can be from serogroups A, B, D, E, and F, the

E4 gene product can be E4-orf6, and the DNA comprising the viral genome can be provided on at least two separate DNA segments. Falck-Pedersen does not teach the use of adenovirus type 35.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Burkhart

Au 1636

DAVID GUZO
PRIMARY EXAMINER